

Application No.: 10/735,602

Docket No.: JCLA10516-R2

**REMARKS****I. Present Status of the Application**

The Office has rejected claims 1-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The Office has rejected claims 1-14 under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (US 6,436,709, referred to hereinafter as "Lin") in view of Tomalia et al. (US Pub. 2002/0013283, referred to hereinafter as "Tomalia").

In response thereto, Applicant has amended independent claims 1 and 11 to describe the claimed invention more explicitly. It is believed that no new matter is added by way of the amendments made to the instant application. After entry of the proposed amendments, Applicant respectfully traverses these rejections for at least the following reasons. It is submitted that the presently pending claims 1-14 are placed in proper condition for allowance, and reconsideration of all pending claims is respectfully requested.

**II. Discussion of Claim Rejections under 35 U.S.C. 112, First Paragraph**

*Claims 1-14 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.*

Regarding the new matter rejection, the Office states that the range of "equal to or lower than 100 psi" recited in claims 1 and 11 is not supported by the application disclosure as originally filed. However, Applicant respectfully disagrees on the reading proposed by the Office.

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According to the disclosure of the specification, the instant invention has disclosed "the contour design of the spray nozzle of the gene gun and modification of the gene gun operation allows the gene gun to operate at a pressure lower than 4 atm. and accelerate the sample solution to an extreme high speed" (paragraph [0009], lines 2-5). The instant application has also disclosed in an embodiment that "[C]onsidering the pressure loss in the whole system, the pressure of the gas after the control valve should be around 90-100 psi, still under the low pressure range of the gas tank" (paragraph [0041], lines 1-3 counted from the end), and the passage in paragraph [0041] describe that the range of the pressure obtained from the calculations is  $P=2.425-4.25$  atm ( $\sim 35.6-62.5$  psi). In addition, the experimental data disclosed in the instant application are practiced under various pressure points, i.e. 50 psi, 60 psi, 80 psi and 100 psi (paragraphs [0056], [0059], [0061], [0063], [0064] and [0070]). Since the instant application has had a mention of "lower than 4 atm ( $\sim 58.8$ psi)" and each single pressure point greater than 4 atm can be practiced, Applicant respectfully submits that "to establish a pressure equal to or lower than 100 psi" recited in claims 1 and 11 is fully supported by the disclosure.

Therefore, it is believed that the disclosure and claims in the prior-filed application are sufficient to comply with the requirements of 35 U.S.C. 112, first paragraph. Accordingly, Applicant asserts that the rejections under 35 U.S.C. 112, first paragraph are no longer proper, and withdrawal of these rejections is respectfully requested.

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**III. Discussion of Claim Rejections under 35 U.S.C. 103**

*Claims 1-14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Lin in view of Tomalia.*

After carefully considering the remarks set forth in this Office Action and the cited references, Applicant has amended independent claims 1 and 11, so as to more clearly define the method according to the instant invention. The supporting ground for the amendments made to claims 1 and 11 can be found at least in FIG. 1 and the description disclosed in paragraphs [0046], [0059] and [0064] of the instant application. As such, Applicant submits that the instant invention, as set forth in claims 1-14, is neither taught, suggested nor disclosed by Lin and Tomalia, or any other cited references, taken alone or in combination, and hereby traverses these rejections as described in detail hereinafter.

The instant invention teaches in amended claims 1 and 11, among other things, “...*wherein the interior contour of the spray nozzle comprises a diverging part, a converging part and a spray neck positioned between the diverging part and the converging part and connected to the material delivery system, wherein the sample solution is released from the material delivery system around the spray neck of the spray nozzle ..., wherein the biological material is delivered without using carriers*”. More specifically, the material delivery system is connected to the spray neck, that is, connected to the transition region between the converging part and the diverging part, such that the sample solution is steadily released as droplets around the spray neck. Due to the contour design of the spray nozzle and the disposition of the material delivery system, the residual sample solution remained in the pressurized chamber can be prevented effectively, so as to enhance the delivering

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efficiency. Moreover, the biological materials can penetrate through the epidermal tissues of animals or the cell membrane and enter into the cytoplasm or the cell nucleus by preparing the sample in the solution without using carriers.

Lin, on the other hand, discloses "[T]he feeding tube sleeve 112 is connected to the pressurized chamber with screws or by welding" (col. 4, lines 1-5) and also discloses "a material delivery system connected to a top part of the pressurized chamber" (claim 1), as shown in FIGs. 1 and 3. In other words, the sample is released from the material delivery system to the pressurized chamber in Lin's teaching, and thus, the sample may be prone to remain in the pressurized chamber. Regarding the delivering effects, the sample cannot be delivered or transformed totally, because the disposition of the material delivery system taught by Lin causes some loss of the sample. Accordingly, Lin substantially fails to teach or suggest the feature "a spray neck positioned between the diverging part and the converging part and connected to the material delivery system, wherein the sample solution is released from the material delivery system around the spray neck of the spray nozzle", as required in proposed independent claims 1 and 11.

According to the experimental data disclosed in the instant application, it is clear that the green fluorescence present on the abdominal epidermis cells and the western blotting results of the mice subjected to DNA solution bombardment using the method described in this invention provides unexpected results and greatly improves the gene transfection, as compared with the method in Lin's teaching. As clearly shown by FIG. 4A of the instant application, the prepared solution includes 0.2  $\mu$ g naked DNA dissolved in the sterile distilled water, and is directly applied to the bombardment with a helium pressure of 60 psi. Almost all the epidermis cells shot by gene

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gun show green fluorescence (the left part of FIG. 4A), and thereby indicating high efficacy for the bombardment of the gene gun.

By contrast, as shown in FIG. 8 in Lin reference, Lin teaches that the bombardment of 10  $\mu$ l of the micro-particles suspension is performed with 100 psi of nitrogen gas (col. 8, lines 1-16). Lin discloses "[T]he suspension is centrifuged briefly and the supernatant is discarded and is re-suspended in 1 ml of sterile distilled water. The re-suspended microcarriers is then vortexed at low speed. During the vortexing, 100  $\mu$ l of DNA (1.0  $\mu$ g/ $\mu$ l), 100  $\mu$ l 0.5 M  $\text{CaCl}_2$  (MERCK 1.02382), and 100  $\mu$ l of 0.05 M spermidine (SIGMA -0266) are added" (col. 6, line 6-col.7, line 6). Accordingly, each bombardment of 10  $\mu$ l micro-particles suspension includes approximate 0.77  $\mu$ g DNA therein. It is noted that the amount of DNA for loaded into the gene gun and the pressure used for shooting the sample in Lin's teaching are both much higher than those of the forgoing experiment disclosed in the instant application.

In general, the transfection efficacy achieved by the method claimed in the instant invention seems to be superior to that taught by Lin, as comparing the results discussed above. It shows that a better transfection efficacy is achieved by the method claimed in the instant invention. Clearly, the above feature of the instant invention indeed has unexpected results when compared with the prior art at the time of filing, and undeniably such feature is not just optimization obvious to one skilled in the art.

Further, Tomalia discloses "a gene transfection particle including a polymer, and genetic material conjugate, with or without a support particle" ([0007]). That is to say, the gene transfection particles taught by Tomalia includes at least the genetic material, and the dendritic

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polymer conjugated with the genetic material. Therefore, Tomalia teaches the gene transfection method involves bombarding cells with the conjugate particles including dendritic polymers, which is quite distinct from the feature "the biological material is delivered without using carriers", as set forth in independent claims 1 and 11.

Since Lin and Tomalia references apparently fail to disclose or teach the technical features set forth in amended independent claims 1 and 11 as discussed above, one of ordinary skill in the art at the time the invention was made CANNOT achieve the method claimed in the instant invention by modifying Lin with the teaching of Tomalia. Consequently, it is strongly believed that the combination of Lin in view of Tomalia is legally deficient to render independent claims 1 and 11 obvious, respectively.

In at least the aforementioned regards, Applicant submits that independent claims 1 and 11 distinctly and patently define over the prior art references, and thus the rejections thereof should be rendered moot. Applicant further respectfully points out that if independent claims 1 and 11 are patentable over the prior art of record, claims 2-10 and 12-14, based on their dependence upon respective claims 1 and 11, are allowable as a matter of law, because these dependent claims contain all features of their base claims.

Hence, favorable consideration of the instant application and withdrawal of these rejections are respectfully solicited.

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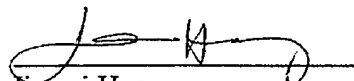
**CONCLUSION**

For at least the foregoing reasons, it is believed that all pending claims are in proper condition for allowance. If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

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